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| (54) Title: SEGMENTALLY DEMINERALIZED BONE IMPLANT | | | |
| | | | |
| (57) Abstract This invention provides a novel unitary bone implant (200) having at least one rigid, mineralized bone segment (201, 202), which may be machined to include threads, grooves, a driver head, a recess or a symmetric or asymmetric shape, and a flexible, demineralized segment (203), which may also be machined to any desired shape prior to demineralization, or after demineralization. The implant (200) of this invention has wide orthopedic applicability, including for repair or replacement of ligaments (300), tendons (400), and joints (800). | | | |

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TITLE OF THE INVENTION
SEGMENTALLY DEMINERALIZED BONE IMPLANT

1.0 Field of the Invention:

5 This invention relates to a device made from segmentally demineralized and appropriately shaped and machined bone for implantation as a ligament, tendon, support or in any other application in which a unitary implant having a first rigid, machined segment and a second, flexible segment, is required.

10 1.1 Background:

There is a continuing need in the art for biologically acceptable ligament or tendon replacements. Various efforts have been made in the art to accommodate this need. For example, in U.S. Patent 5,053,049, a flexible prosthesis of predetermined shape and a process for making said prosthesis was disclosed. According to that disclosure, a flexible
15 biocompatible and non-antigenic prosthesis for replacement of a cartilaginous part was prepared by machining bone into a desired shape corresponding to the shape of a cartilaginous body part to be replaced, demineralization of the bone to impart flexibility, and tanning to reduce antigenicity. There was no disclosure or suggestion of using the demineralized bone as a tendon or ligament replacement.

20 In U.S. Patent No. 5,092,887, a method for replacement or augmentation of a damaged fibrous connective tissue was disclosed wherein a ligament made from a segment of bone that had been demineralized was attached between first and second body parts. There was no disclosure or suggestion of machining the bone prior to demineralization to
25 produce fixation ends thereon, and demineralization of only a segment of the thus machined bone to produce a flexible segment, while leaving the machined attachment ends in a fully mineralized and rigid state for fixation directly to bone adapted to receive such fixation ends. The disclosure in the 5,092,887 patent with respect to its discussion of background art and methods of demineralization of bone is hereby incorporated by
30 reference.

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2.0 SUMMARY OF THE INVENTION

This invention provides a novel unitary bone implant having at least one rigid, mineralized bone segment, which may be machined to include threads, grooves, a driver
5 head, a recess or a symmetric or asymmetric shape, and a flexible, demineralized segment, which may also be machined to any desired shape prior to demineralization, or after demineralization.

3.0 BRIEF DESCRIPTION OF THE DRAWINGS

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Figure 1 provides a view of a first embodiment of the implant of this invention in which a rigid bone segment is machined to exhibit threads on each end (figure 1A), and which is then demineralized only in the internal section to provide a flexible segment between the machined ends (figure 1C); figure 1B provides a view of an alternate embodiment in which
15 one end of the implant has a rigid fixation bone block; figure 1D shows an end-on view of a cannulated embodiment of the implant of this invention.

Figure 2 provides a view of a second embodiment of the implant of this invention in which a rigid bone segment is machined to exhibit threads on one end and an attachment hole at
20 the other (figure 2A), and which is then demineralized on the attachment hole end of the implant to provide a flexible segment, while retaining the threaded segment as a rigid member (figure 2B). A partial cannulation of the implant is shown in end-on (fig. 2C), top (fig. 2D) and side views (fig. 2E).

25 Figure 3 provides a view of a third embodiment of the implant of this invention in which a rigid bone segment is machined to exhibit a fixation block at each end of the implant (figure 3A), and which is then demineralized between the two ends to provide a flexible segment between the machined fixation block ends (figure 3B).

30 Figure 4 provides a view of a fourth embodiment of the implant of this invention in which a rigid bone segment is machined to exhibit a fixation block at one end and an attachment hole (figure 4A) or several holes or perforations (figure 4B) at the other, and which is then

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demineralized at the end bearing the attachment hole(s) (figures 4C and 4D) to provide a flexible segment, while retaining the fixation block end as a rigid member.

Figure 5 shows one method of implantation of the implant of this invention in which
5 fixation screws are utilized to retain the implant of this invention in place either by locking the implant in place through holes in the rigid segment of the implant (figure 5A), or by locking the implant into place at the rigid end of the implant via a tapped recess (figures 5B and 5C).

10 Figure 6 shows an embodiment of this invention in which the implant is a femoral ring in which the upper and lower ends of the ring are retained in a rigid, mineralized state and which may be machined to exhibit a thread or a groove, and the internal segment of the implant is demineralized to exhibit a soft spongy layer to provide flexible support upon
insertion of this embodiment of the invention between adjacent vertebral bodies.

15 Figure 7 shows various cross-sections for the demineralized segment of the implant of this invention.

Figure 8 depicts one embodiment of a prosthetic joint according to this invention.
20

4.0 DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

This invention provides a biologically acceptable ligament, tendon, support or other implant for replacement of damaged ligaments, tendons, vertebral disks and the like,
25 wherein there is a need for an implant having both a rigid machined portion or segment as well as a flexible, demineralized portion or segment. According to one embodiment of this invention, a segment of preferably cortical bone is machined into a desired shape, with at least one end being machined so as to provide a means for fixation of that end directly to a bone machined in a complementary fashion.

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Referring to figure 1A, a first embodiment of the implant of this invention **100** is shown in which the ends **101** and **102** of the implant are machined so as to exhibit a thread.

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and the bone to which the implant is to be affixed is tapped to exhibit a receiving thread complementary to the thread on the implant end. Alternatively, the threaded ends **101**, **102** may be self-tapping, thereby eliminating the need to tap the receiving bone. A simple hole, of a diameter slightly smaller than the diameter of the threaded implant ends, may be drilled or produced by like means to receive the threaded implant end. An internal segment **103** of the implant is demineralized to provide a flexible segment of the implant, while transition zones **104**, **105** are provided wherein the level of mineralization of the bone gradually changes from a fully mineralized to a demineralized state. In a preferred version of this embodiment of the invention, the two ends **101**, **102** of the implant are machined to exhibit threads such that clockwise or counterclockwise rotation of the entire implant results in simultaneous insertion of both ends of the implant or extraction of both ends of the implant into or out of complementarily machined bones to which the implant is to be affixed, without kinking of the flexible segment **103** of the implant. In figure 1B, an alternate embodiment is shown wherein one of the ends, **101'**, is not threaded, but is machined to any desirable shape, such as a fixation block, such that the threaded end **102** may be threaded into the receiving bone, while the fixation block **101'** is affixed in place by interference screws or like means known in the art. In yet a further embodiment, shown in figure 1D, the entire implant is machined so as to exhibit a cannulation **110** throughout its length or a portion thereof. In this fashion, the implant may be inserted over a guide-wire or like guide means. Alternatively, the aspect **110** may be an internal thread capable of receiving a threaded retention screw. It will be recognized that features disclosed for this embodiment or any of the other embodiments of the invention may be applied to other embodiments of this invention, to produce embodiments exhibiting a variety of combinations of different features disclosed for each of the individually disclosed embodiments.

In a further embodiment of this invention **200** shown in figure 2, only one end **202** of the implant **200** is machined to exhibit a thread or another machined feature, while the other end **201** may be machined to exhibit a fixation hole **210** or a similar feature, which permits for suturing or otherwise fixing that end to a ligament or a tendon. A transition zone **204** from a mineralized to a demineralized state is provided, as is a flexible segment of the implant **203**. In figures 2C-E, there are shown an end-on view, a side view and a

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top view, respectively. In this embodiment of the invention, an optional cannulation 220 is shown, permitting threading of the machined portion 202 of the implant over a guide-wire, for example, while not interfering with the flat, demineralized segment 203 of the implant.

5 In a further embodiment 300 of this invention shown in figure 3, the implant may be used to replace a ligament. In this embodiment, two transition zones 304, 305 from the flexible segment 303 to terminally mineralized fixation blocks 301, 302 are provided. The fixation blocks 301 and 302 each have a canal 306, 307 machined therein for receiving a fixation screw or pin. The mineralized sections 302, 303 may be machined into any
10 desired form of an anchoring fixture. The anchoring fixture may contain a screw thread, a hole for receipt of an anchoring pin or an anchoring screw, or a screw that rotates within a sleeve.

In the embodiment 400 shown in figure 4A, the implant is used for repair or
15 replacement of a tendon. In this embodiment, only one end 402 of the implant 400 is machined for fixation in a bone, and the second end 401 of the implant is adapted to a variety of shapes, terminating in a means, such as a threadable hole 410, for fixation of that end to bone, muscle, tendon or ligament. In an alternate embodiment shown in figures 4B and 4D, the end 401' is machined to exhibit a plurality of holes or perforations, 410', such
20 that end 401' may be sutured to a receiving biological structure, such as a muscle, ligament, tendon, bone or the like.

In figure 5, one method of implantation of the implant 500 of this invention is shown in which fixation screws 553 are utilized to retain and embodiment of the implant
25 500 of this invention in a machined slot 551 in a bone 550 either by locking the implant in place (figure 5A) through holes 552 in the rigid segment 501 of the implant (figure 5A), or by locking the implant into place at the rigid end 503 of the implant via a tapped recess (figures 5B and 5C). The other end of the implant 504 is demineralized, and is thus flexible, and terminates in a hole 502 or other fixation means by which that end of the
30 implant is attached to bone, tendon, ligament or muscle. As noted above, section 501 could be threaded, end 502 could be retained in a mineralized state and could be shaped as a fixation block for retention by an interference screw, or threaded. In addition, the implant

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500 may be cannulated, with the recess 503 continuing through the entire length of the implant, or some portion thereof.

Figure 6 shows an embodiment of this invention in which the implant 600 is a femoral ring member in which the upper and lower ends 601, 604 are retained in a rigid, mineralized state and which may be machined to exhibit a thread or a groove by means known in the art (see WO 97/25945, hereby incorporated by reference for this purpose). The internal segment of the implant 603 is demineralized to exhibit a soft spongy region to provide flexible support upon insertion of this embodiment of the invention between, for example, adjacent vertebral bodies. An internal canal 601 is shown in the femoral ring, which derives from the natural intramedullary canal of the bone from which the femoral ring is obtained by substantially planar, parallel cross-cuts across the diaphysis of a femur or like long bone.

The implant of this invention comprising a unitary machined, segmentally demineralized bone comprising a first mineralized portion or segment, and a second, flexible, demineralized portion or segment is produced by machining a piece of preferably cortical bone into any desired shape. The bone is preferably chosen to be strong cortical bone, such as from the femur, tibia, fibula, radius or ulna. The source of the donor bone may be autograft, allograft or xenograft bone, with the appropriate cautionary steps known in the art being taken in each case to prevent introduction into the recipient of pathogenic or antigenic agents.

After appropriately shaping the implant bone stock, a segment of the implant is preferably machined to exhibit a thread or like fixation means whereby the implant may be directly affixed to recipient bone machined in a complementary fashion. That segment of the implant is retained in a mineralized state, by appropriately protecting that segment of the implant with any protective device, such as with parafilm, a rubber or latex covering, plastic wrap, and the like. The remaining segment of the implant is then demineralized according to methods known in the art. For example, in the embodiment 100 of this invention shown in figure 1A, both ends 101, 102 may be inserted into rubber stoppers spanning the transition zones 104, 105, and the internal segment 103, is exposed to an acid

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solution of sufficient strength to leach the minerals from that segment of the bone. A 5% acetic acid solution or a 1 N hydrochloric acid solution may be employed, and the implant checked periodically for the desired level of flexibility of the internal zone 103. It is important that an excessively high concentration of strong acid not be employed for this process, as this will result in cleavage of the peptide bonds of the collagenous matrix within which the minerals are deposited. Accordingly, HCl concentrations of between about 0.1N to 2N are acceptable, with the period of exposure to acid being increased for the lower acid concentrations and decreased for the higher acid concentrations. Likewise, depending on the strength of the acid used. The transition zones 104, 105 are formed by diffusion of the acid into and diffusion of the minerals out of the bone in that segment of the implant covered by the protective covering. By varying the degree of demineralization, the properties of the implant of this invention may be altered to provide optimal strength and flexibility, as required for the particular application for which the implant is to be employed.

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The thus treated implant may be further treated by tanning or other means known in the art to reduce the antigenicity of the implant. For example, glutaraldehyde treatment (see U.S. Patent No. 5,053,049, hereby incorporated by reference for this purpose), may be used.

20

In figure 7, various cross-sectional shapes of the implant of this invention are shown. Thus, in figure 7A, a cylindrical cross-section is shown. It will be recognized that various diameters, from as small as 0.5 mm or smaller to as large as 10 mm, or in certain applications, even larger, may be desirable. In figure 7B, an oval cross-section is provided. In figure 7C, a flat cross section is provided. In figure 7D, a cross-shaped cross-section is provided. Those skilled in the art will recognize that the disclosure of this invention permits for essentially any desirable shape to be generated for the flexible or rigid segments of the implant of this invention, and such variations come within the scope of this disclosure and the appended claims. In forming the various cross-sectional shapes suggested herein, it is desirable that a smooth transition occurs between the rigid end(s) of the implant and the flexible segment. This is accomplished by appropriately machining the end(s) such that a taper into the flexible segment occurs, and by carefully controlling the

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demineralization process to ensure a graded demineralization from the fully mineralized segment to the demineralized segment.

It will further be understood from the foregoing disclosure that the implant of this invention may be appropriately fashioned for a wide diversity of applications. For example, an implant of this invention may be applied to repair of ligaments or tendons in the hand, elbow, knee, foot, ankle or any other anatomical location as needed. Furthermore, the implant of this invention may be applied to replacement any of a variety of joints. Methods and implant shapes known in the art for joint replacement, (see, for example U.S. Patent Nos. 4,871,367; Des. 284,099; Des. 277,784; Des. 277,509; 3,886,600; 3,875,594; 3,772,709; 5,484,443; 5,092,896; 5,133,761; 5,405,400; and 4,759,768; all of which are herein incorporated by reference for their teachings of various considerations applicable to joint prosthetic implants), may be fashioned according to and replaced by the implant of the instant disclosure. Thus, in one embodiment of this invention, a piece of cortical bone is shaped so as to form a surgically implantable prosthetic joint having a load distributing flexible hinge, analogous to that disclosed in U.S. Patent 3,875,594 (which was made from molded silicone rubber). According to this embodiment of the invention, a prosthesis is formed consisting of an enlarged midsection, and a pair of oppositely projecting distal and proximal stem portions. The volar aspect of the midsection is machined to exhibit an indent or transverse channel extending across its width, to form the flexible hinge upon demineralization of the midsection. The midsection, intended to act as the hinge, is demineralized, and the mineralized extremities of the implant are retained in a mineralized state for insertion of each end into the intramedullary space of the bones adjacent to the joint which the implant replaces. The mineralized extremities are machined to exhibit a thread or a ratcheting tooth structure, such that upon insertion of each end into the intramedullary space of the adjacent bones, the end is fixed in place. Since the ends are made from bone, the natural process of fusion between the implant and the bone into which it is inserted occurs over several weeks, thus permanently fixing the prosthesis into position and preventing any movement of the ends of the implant. Implants according to this embodiment of the invention may be used, for example, to replace metacarpophalangeal joints, proximal interphalangeal joints and the like. Accordingly, this invention represents a significant advance in the art as it provides a

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natural alternative to currently employed metallic, hydroxyapatite, silastic, silicone or like elastomeric materials for joint arthroplasty.

In figure 8, there is provided one diagrammatic representation of an implant of a
5 prosthetic joint according to this invention and which may be prepared according to the
concepts central to the instant invention. The implant 800 has an enlarged midsection 810
which is demineralized up to and including a portion of the transition segment 820. On
either side of the midsection 810 are mineralized projections 830 adapted for insertion into
the intramedullary canals of bones adjacent to the joint which the implant 800 replaces. A
10 groove or channel 850 is provided to act as the hinge and to allow bending motion of the
joint according to principles described in U.S. Patent No. 3,875,594, herein incorporated by
reference for this purpose. Optionally, the projections 830 may exhibit an external feature
designed to enhance retention of the implant in the intramedullary spaces. In the
embodiment shown in figure 8, this feature is shown as a tooth-like serration which may be
15 machined into an upper or lower aspect of each projection 830 or which may project
around the circumference of the projections. Alternate external features which may aid in
retention of the implant include holes through which retention pins may be inserted,
grooves, ribbing and the like. The demineralized midsection 810 permits the implant 800
sufficient flexibility to allow that portion of the implant to act as a joint, while the
20 projections 830 fuse with the bone into which they are inserted to form a permanent
fixation.

Having now generally described various embodiments of this invention, the
following examples are provided by way of further exemplification of this invention. It
25 should be recognized that the invention disclosed and claimed herein is not to be limited to
the specifics provided in these examples:

Example 1

MACHINING OF THE IMPLANT OF THIS INVENTION:

30 The starting bone stock was chosen such that a piece of bone consisting
substantially of cortical bone was used to machine the implant of this invention. Implants
from the linea aspera of the femur or an anterior aspect of the tibia were used for this

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purpose, but other cortical sources of bone would be acceptable. The desired bone segment was removed with a bone saw or a water-cooled diamond core cutter, and trimmed to fit in a lathe for machining of desired external features. The bone was first machined to a known diameter and length. The ends were then machined to exhibit an internal thread, an
5 external thread, or to have one machined end while the other end of the implant was drilled to exhibit one to several holes. The internal segment destined for demineralization was then either retained in a cylindrical form or machined in a milling machine or a grinder, to exhibit a flat internal segment, or another desired shape, between the threaded ends or the fixation ends.

10

Example 2

SEGMENTAL DEMINERALIZATION OF MACHINED BONE GRAFTS

1. Large Cylindrical Ligament Repair Grafts:

Demineralization of a machined large cylindrical ligament repair graft was
15 completed in three days using approximately 40 mL of 0.75M-1.0M hydrochloric acid solution. The implant was exposed to fresh solution at least once per day. In order to produce a gradual transition from a fully mineralized end to a fully demineralized segment, the point of contact of the HCl solution with the implant was varied over the duration of the demineralization process.

20

2. Small Cylindrical Ligament Repair Grafts:

Demineralization of a machined small cylindrical ligament repair graft was
completed in two days using approximately 40 mL of 0.75M-1.0M hydrochloric acid
solution. The implant was exposed to fresh solution at least once per day. In order to
25 produce a gradual transition from a fully mineralized end to a fully demineralized segment, the point of contact of the HCl solution with the implant was varied over the duration of the demineralization process.

3. Flat Ligament or Tendon Repair Grafts:

30 Demineralization of a machined ligament or tendon repair graft wherein an internal segment of the graft was machined flat, was completed in twenty-four hours using approximately 40 mL of 0.75M-1.0M hydrochloric acid solution. The implant was

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exposed to fresh solution at least once per day. In order to produce a gradual transition from a fully mineralized end to a fully demineralized segment, the point of contact of the HCl solution with the implant was varied over the duration of the demineralization process.

5 4. Double Flat Ligament Repair Grafts Having Two Rigid Ends:

Demineralization of a machined, flat ligament repair graft was completed in twenty-four hours using approximately 40 mL of 0.75M-1.0M hydrochloric acid solution. The implant was exposed to fresh solution at least once per day. In order to produce a gradual transition from a fully mineralized end to a fully demineralized segment, the point of
10 contact of the HCl solution with the implant was varied over the duration of the demineralization process. In order to protect both rigid ends of the implant, one bearing a thread and the other being a fixation block, the implant was exposed to the acid solution only in the middle segment by keeping the threaded end of the implant above the meniscus of the acid, and the fixation block end of the implant was inserted into a bored-out stopper,
15 which also acted as a plug at the bottom of the acid container, into which a hole adequate to receive the implant bearing stopper had been drilled.

In view of the foregoing disclosure and examples, in which various embodiments of the implant of this invention are disclosed and described, including the best mode, the
20 following claims are provided to define the scope of this invention. Those skilled in the art will recognize that various modifications on the specifics of the invention disclosed herein come within the scope of the appended claims.

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WHAT IS CLAIMED IS:

- 1 1. A segmentally demineralized bone implant comprising a first mineralized
2 segment, and a second, flexible, demineralized segment.
- 1 2. The implant of claim 1 wherein said mineralized or demineralized segment
2 is machined to exhibit a desired feature selected from a groove, an external
3 thread, an internal thread, a driver head, a recess and a symmetric or
4 asymmetric shape.
- 1 3. The implant of claim 2 comprising at least one machined, mineralized end
2 or segment, adapted for fixation of said implant to or in bone, and a
3 demineralized segment of sufficient flexibility to act as a ligament, tendon,
4 or flexible support, when said implant is affixed between first and second
5 body parts.
- 1 4. The segmentally demineralized bone implant of claim 1 further comprising
2 a zone between said mineralized segment and said demineralized segment,
3 wherein a gradual transition from mineralized to demineralized bone occurs.
- 1 5. The segmentally demineralized bone implant of claim 2 comprising two
2 machined, mineralized ends adapted for fixation of said implant to bone
3 adapted to receive said machined mineralized ends of said implant, and
4 wherein said demineralized segment extends between said two machined,
5 mineralized ends.
- 1 6. The segmentally demineralized bone implant of claim 1 wherein said
2 mineralized segment forms an end of the implant and which is machined to
3 exhibit an external thread, a hole, or an internal thread, for receiving a
4 retention screw, retention pin, sutures or threading, and wherein said

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5 implant is affixed to bone adapted to receive said machined mineralized end
6 or said demineralized segment of said implant.

1 7. The segmentally demineralized bone implant of claim 4 comprising two
2 machined, mineralized ends, wherein each said end is machined to exhibit a
3 thread, a self-tapping thread, a hole for receipt of a retention pin or screw, or
4 an internal thread for receipt of a retention screw, and wherein bone to
5 which said implant is to be affixed is adapted to receive said implant.

1 8. The segmentally demineralized bone implant of claim 5 wherein said thread
2 of each said end is defined such that either clockwise or counterclockwise
3 rotation of said implant results either in simultaneous insertion of both ends
4 into or extraction of both ends from bone adapted to receive said implant.

1 9. The segmentally demineralized bone implant of claim 1 wherein said at
2 least one machined, mineralized end is adapted for fixation of said implant
3 to bone machined in a complementary fashion, and wherein said
4 demineralized segment having sufficient flexibility to act as a ligament or
5 tendon terminates in a demineralized segment adapted for fixation of said
6 demineralized segment to a bone, muscle, tendon or ligament.

1 10. The segmentally demineralized bone implant of claim 1 affixed between a
2 first and a second bone, between a bone and a muscle, between a bone and a
3 tendon, or between a bone and a ligament.

1 11. The implant of claim 1 in the shape of a dowel or femoral ring, said implant
2 having two cortical ends and an internal region of soft, flexible,
3 demineralized bone.

1 12. The implant of claim 11 wherein a canal is present in the implant.

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- 1 13. The implant of claim 11 when inserted between adjacent vertebral bodies.
- 1 14. The implant of claim 1 which is cannulated throughout the implant or
2 through a portion of the implant.
- 1 15. An improved method for the replacement or augmentation of a damaged
2 fibrous connective tissue in a region between first and second body parts,
3 comprising attaching an elongated artificial ligament or tendon made from
4 demineralized bone between said first and second body parts, said artificial
5 ligament having both compliant elasticity and high longitudinal strength
6 such that it has sufficient flexibility to allow it to be shaped to conform to
7 the configuration of the region to be repaired, the improvement comprising
8 machining at least one end of the bone prior to segmental demineralization
9 to produce at least one fixation end thereon which end is not demineralized,
10 and demineralization of a segment of the thus machined bone to produce a
11 flexible segment.
- 1 16. The method of claim 15 wherein said artificial ligament or tendon
2 comprises two machined mineralized ends and an intermediate, flexible,
3 demineralized segment.
- 1 17. A method for the replacement or augmentation of a damaged ligament or
2 tendon comprising attaching a machined segmentally demineralized bone
3 implant between a first and a second bone, between a bone and a ligament
4 on a second bone, or between a bone and a tendinous segment of a muscle.
- 1 18. A method for making a tendon or ligament implant which comprises
2 machining a segment of substantially cortical bone into any desired shape,
3 machining at least one end thereof for fixation directly to bone, and
4 segmentally demineralizing a segment of said substantially cortical bone
5 such that said demineralized segment acquires sufficient flexibility and
6 elasticity to act as a tendon or ligament replacement.

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- 1 19. An implant prepared according to the method of claim 18.
- 1 20. The implant according to claim 1 comprising a flexible, demineralized
2 midsection and two mineralized projections.
- 1 21. The implant of claim 20 wherein said mineralized projections exhibit an
2 external feature selected from serrated edges, threads, and ribbing.
- 1 22. A prosthetic joint implant comprising cortical bone having a load
2 distributing flexible hinge consisting of an enlarged midsection of
3 demineralized bone, and a pair of oppositely projecting distal and proximal
4 stem portions consisting essentially of mineralized bone.
- 1 23. The prosthetic joint of claim 22 wherein the volar aspect of said midsection
2 is machined to exhibit an indent or transverse channel extending across its
3 width.
- 1 24. The prosthetic joint of claim 23 wherein said oppositely projecting distal
2 and proximal stem portions are inserted into the intramedullary space of
3 bones adjacent to the joint which the implant replaces.
- 1 25. The prosthetic joint of claim 24 wherein said mineralized extremities are
2 machined to exhibit an external thread, an internal thread, a hole or series of
3 holes to receive a retention pin or a series of retention pins, a serrated edge,
4 or a ratcheting tooth structure, such that upon insertion of each end into the
5 intramedullary space of the adjacent bones, the end is fixed in place.
- 1 26. A method of joint arthroplasty which comprises replacement of a
2 metacarpophalangeal joint, a proximal interphalangeal joint, or like joint
3 with an implant comprising a segmentally demineralized bone.

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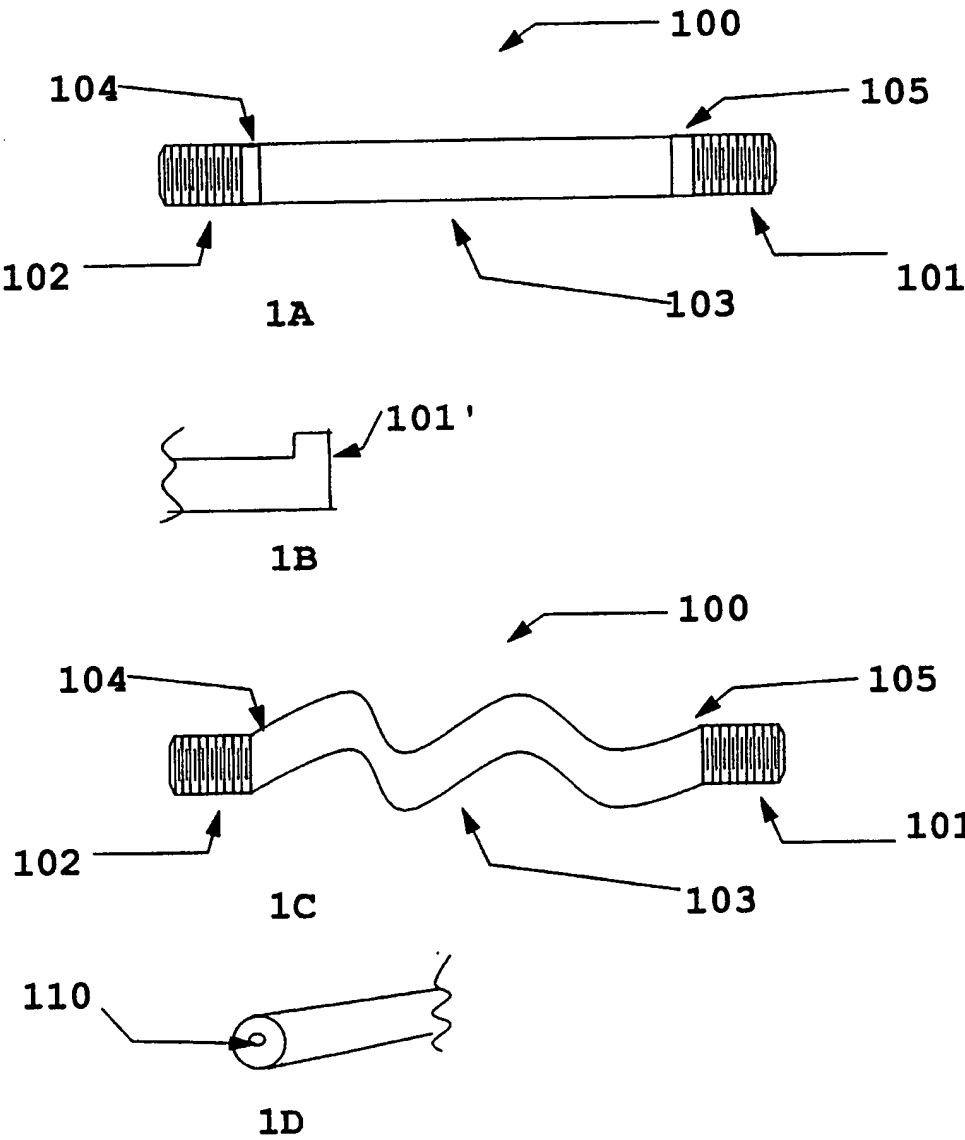


FIGURE 1

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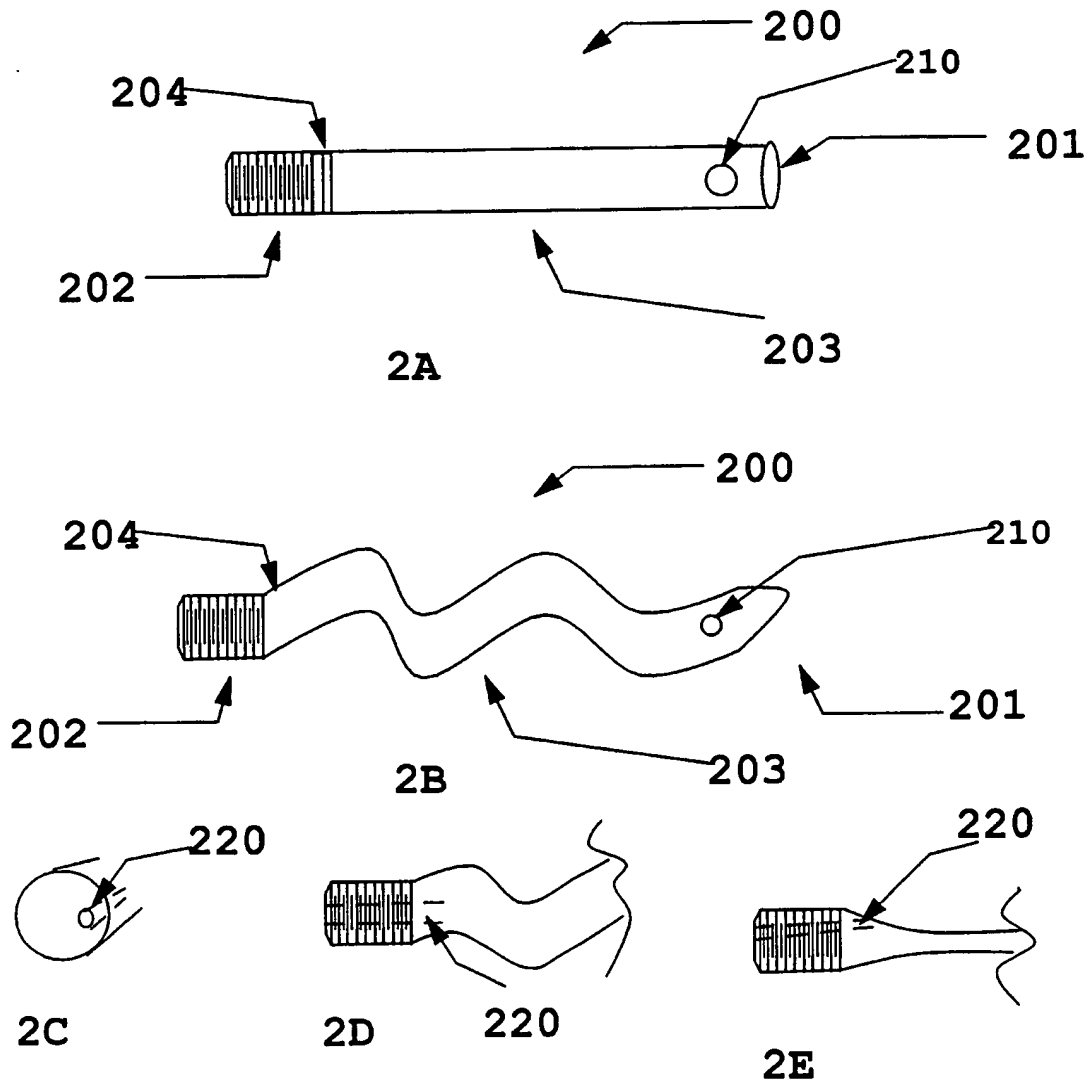
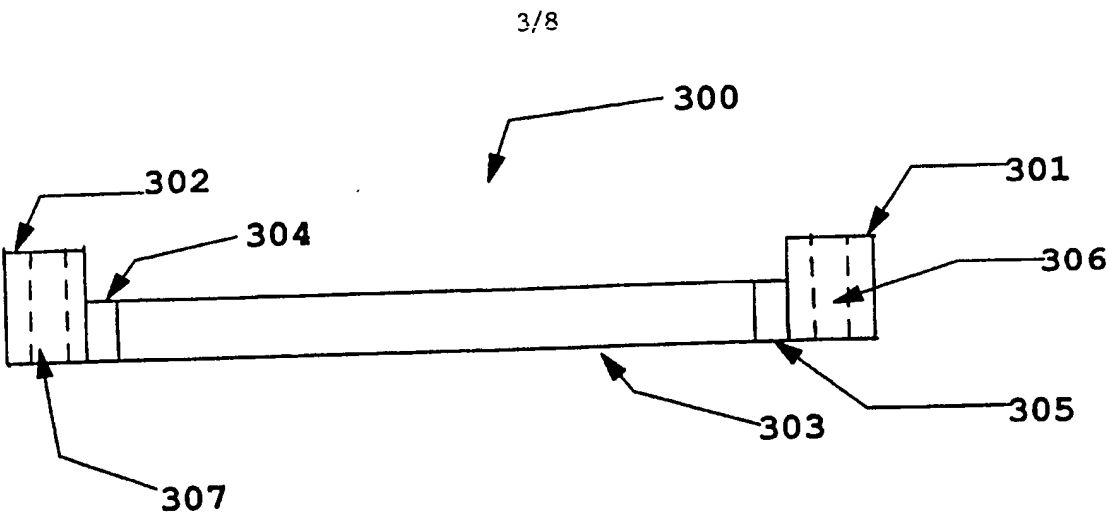


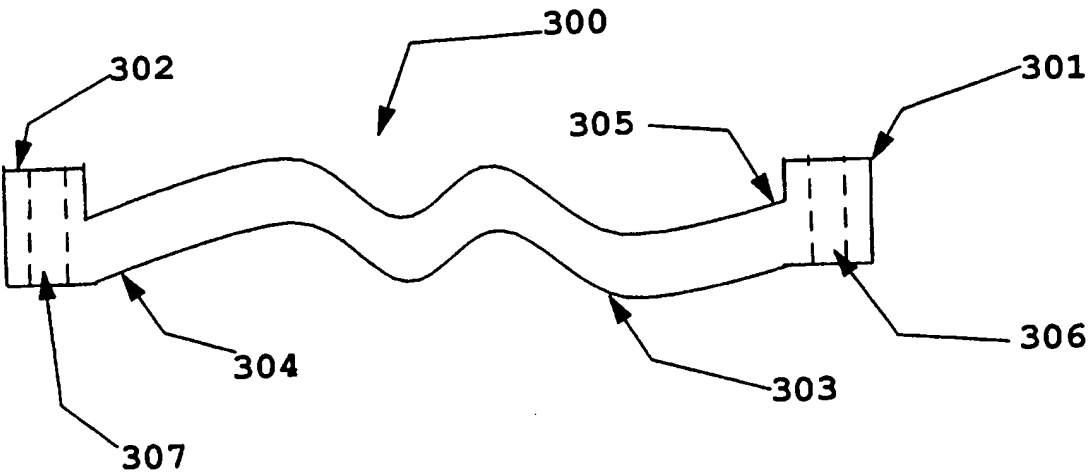
FIGURE 2

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3A



3B

FIGURE 3

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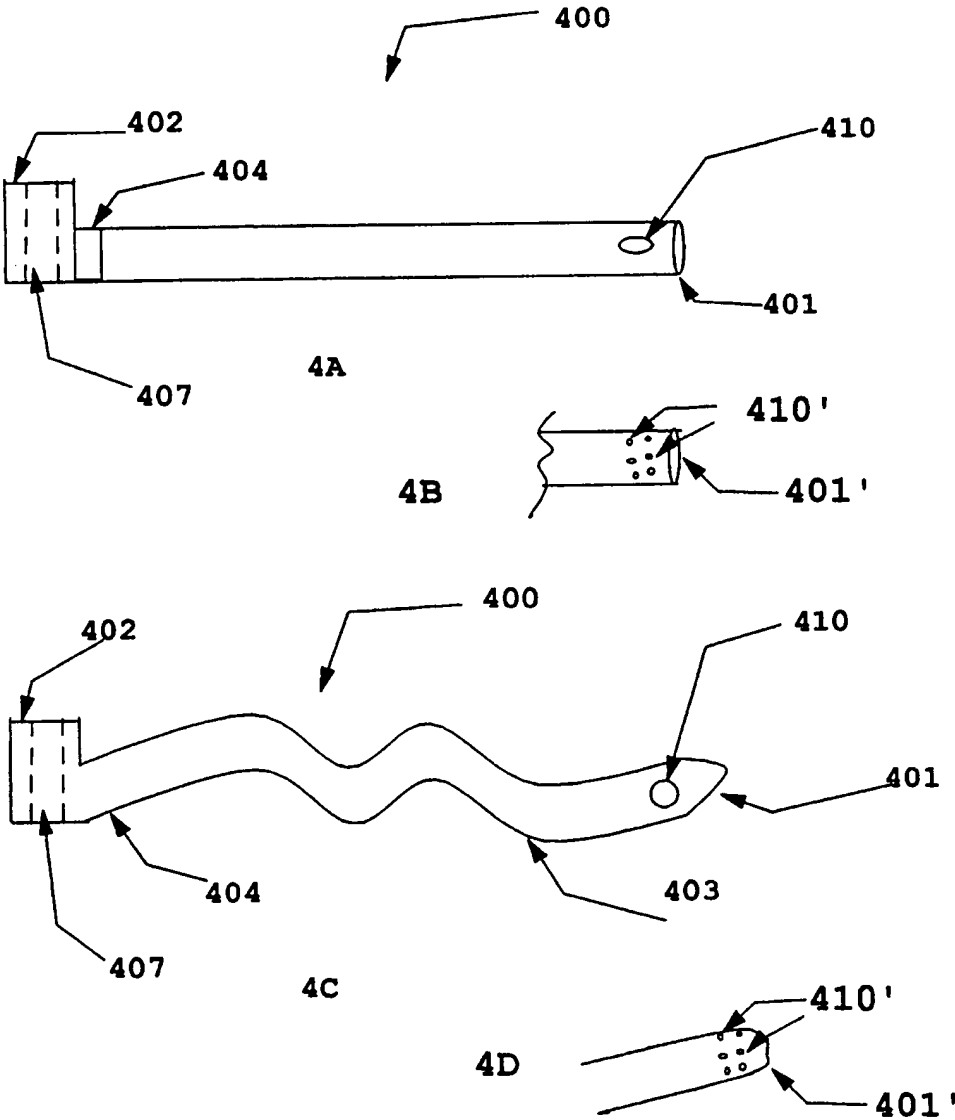


FIGURE 4

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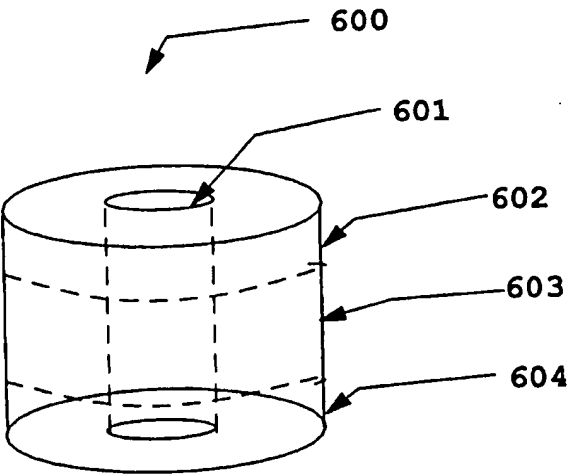


Figure 6

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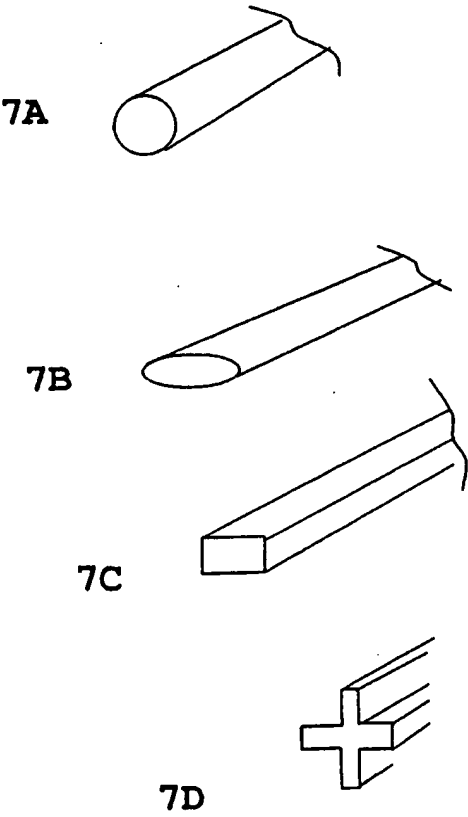


Figure 7

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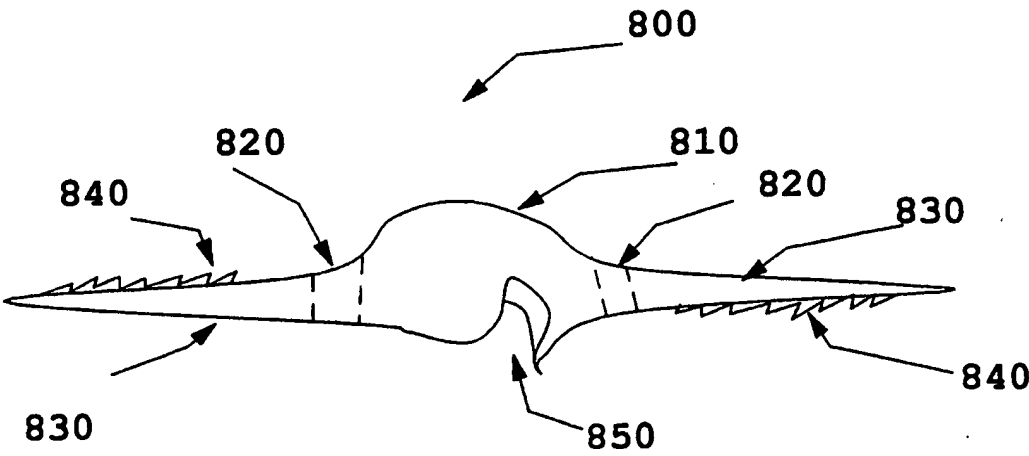


Figure 8

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 98/21530

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61F2/28 A61L27/00 A61F2/08 A61F2/42

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61F A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|------------------------------------|
| X Y | US 4 627 853 A (CAMPBELL) 9 December 1986 see the whole document | 1 2,3,5,6, 9,10,14, 18,19 |
| Y A | US 4 772 286 A (GOBLE) 20 September 1988 see the whole document | 2,3,5,6, 9,10 7 |
| Y A | WO 97 25945 A (UNIVERSITY OF FLORIDA, TISSUE BANK) 24 July 1997 cited in the application see the whole document | 14 2,6,11, 21,25 |
| | --- | |
| | --- -/-- | |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

18 March 1999

Date of mailing of the international search report

25/03/1999

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| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|--|-----------------------|
| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| Y | US 5 092 887 A (GENDLER) 3 March 1992 cited in the application | 18,19 |
| A | see abstract; claim 1 see column 5, line 51 - column 6, line 4 --- | 1,3,9,10 |
| A | US 5 053 049 A (CAMPBELL) 1 October 1991 cited in the application see the whole document --- | 1,18,22 |
| A | EP 0 483 944 A (GENDLER) 6 May 1992 see the whole document --- | 1,22 |
| A | US 5 676 146 A (SCARBOROUGH) 14 October 1997 see column 1, line 30 - line 39; claims 4,6; examples 1,4 --- | 1 |
| A | US 5 192 322 A (KOCH) 9 March 1993 see the whole document --- | 3,5,9, 10,20 |
| A | US 4 553 272 A (MEARS) 19 November 1985 see figure 2 --- | 4 |
| A | US 4 839 215 A (STARLING) 13 June 1989 see figures 1-3 --- | 11,12 |
| A | EP 0 356 112 A (JOHNSON & JOHNSON ORTHOPAEDICS) 28 February 1990 see figures 1-3 --- | 11,13 |
| A | WO 97 25941 A (OSTEOTECH) 24 July 1997 see the whole document --- | 18 |
| A | US 3 875 594 A (SWANSON) 8 April 1975 cited in the application see the whole document --- | 22-24 |
| A | US 4 743 259 A (BOLANDER) 10 May 1988 --- | |
| A | WO 93 15694 A (BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM) 19 August 1993 ----- | |

INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/US 98/21530

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---------------------|---|--|
| US 4627853 A | 09-12-1986 | CA 1298935 A DE 3617897 A FR 2582517 A GB 2175506 A,B JP 62032965 A | 21-04-1992 04-12-1986 05-12-1986 03-12-1986 12-02-1987 |
| US 4772286 A | 20-09-1988 | CA 1336058 A JP 1314559 A AU 606949 B AU 1618288 A EP 0342281 A US RE34293 E | 27-06-1995 19-12-1989 21-02-1991 16-11-1995 23-11-1989 22-06-1993 |
| WO 9725945 A | 24-07-1997 | US 5814084 A AU 1700597 A CA 2243152 A EP 0876129 A PL 328226 A | 29-09-1998 11-08-1997 24-07-1997 11-11-1998 18-01-1999 |
| US 5092887 A | 03-03-1992 | NONE | |
| US 5053049 A | 01-10-1991 | DE 3617898 A FR 2582516 A GB 2175807 A,B JP 62032966 A | 04-12-1986 05-12-1986 10-12-1986 12-02-1987 |
| EP 483944 A | 06-05-1992 | DE 69111021 D ES 2076467 T US 5306304 A US 5464439 A US 5556430 A | 10-08-1995 01-11-1995 26-04-1994 07-11-1995 17-09-1996 |
| US 5676146 A | 14-10-1997 | AU 4270397 A WO 9810712 A | 02-04-1998 19-03-1998 |
| US 5192322 A | 09-03-1993 | AT 98857 T DE 59003969 D EP 0437174 A | 15-01-1994 03-02-1994 17-07-1991 |
| US 4553272 A | 19-11-1985 | NONE | |
| US 4839215 A | 13-06-1989 | AU 606603 B AU 7544887 A CA 1307742 A DE 3790291 C EP 0310623 A GB 2212488 A,B JP 1502642 T JP 2760793 B WO 8707495 A | 14-02-1991 11-01-1988 22-09-1992 26-06-1997 12-04-1989 26-07-1989 14-09-1989 04-06-1998 17-12-1987 |
| EP 356112 A | 28-02-1990 | AT 98859 T AU 624627 B AU 3947989 A CA 1328957 A DE 68911622 D DE 68911622 T DK 405189 A | 15-01-1994 18-06-1992 22-02-1990 03-05-1994 03-02-1994 07-04-1994 19-02-1990 |

INTERNATIONAL SEARCH REPORT

information on patent family members

Int. J. Application No

PCT/US 98/21530

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---------------------|--|--|
| EP 356112 A | | ES 2048290 T FI 893880 A GR 89100516 A JP 2224660 A PT 91482 A,B US 5545229 A US 5171281 A | 16-03-1994 19-02-1990 22-08-1990 06-09-1990 08-03-1990 13-08-1996 15-12-1992 |
| WO 9725941 A | 24-07-1997 | AU 1535097 A CA 2243365 A EP 0880345 A | 11-08-1997 24-07-1997 02-12-1998 |
| US 3875594 A | 08-04-1975 | AT 344308 B AT 688474 A AU 7237874 A BE 819173 A CA 1019901 A DE 2440103 A FR 2242067 A GB 1442022 A JP 910681 C JP 50055195 A JP 52040797 B MX 3390 E NL 7411319 A,B SE 398043 B SE 7410687 A | 10-07-1978 15-11-1977 19-02-1976 26-02-1975 01-11-1977 24-07-1975 28-03-1975 07-07-1976 14-06-1978 15-05-1975 14-10-1977 27-10-1980 03-03-1975 05-12-1977 28-02-1975 |
| US 4743259 A | 10-05-1988 | US 4902296 A | 20-02-1990 |
| WO 9315694 A | 19-08-1993 | AU 3619293 A CA 2117379 A DE 69307299 D EP 0625891 A HK 71597 A JP 7503869 T US 5607474 A US 5876452 A | 03-09-1993 19-08-1993 20-02-1997 30-11-1994 06-06-1997 27-04-1995 04-03-1997 02-03-1999 |